Translation

PCT/JP2003/010131

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A31454	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/JP2003/010131	International filing date (*day/month/year*) 08 August 2003 (08.08.2003)	Priority date (*day/month/year*) 08 August 2002 (08.08.2002)
International Patent Classification (IPC) or national classification and IPC C12N 15/00, 15/12, 15/19, C12Q 1/02, 1/66, 1/68, A61K 45/00, 39/395, A61P 9/10, 29/00, 43/00		
Applicant RIKEN		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
08 August 2003 (08.08.2003)	23 March 2004 (23.03.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/JP2003/010131

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☐ the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the claims:

pages _____, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the drawings:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

☐ the sequence listing part of the description:

pages _____, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP03/10131

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 15, 23-26

because:

☒ the said international application, or the said claims Nos. 23-25 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The subject matters of claims 23-25 relate to a method for treatment of the human or animal body by therapy, which does not require an international preliminary examination by the International Preliminary Examining Authority in accordance with PCT Article 34(4)(a)(i) and Rule 67.1(iv).

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 15, 26 are so unclear that no meaningful opinion could be formed *(specify)*:

Even when the statement in the description is taken into consideration, what compounds are included and what are not in "the transcriptional activity inhibitor" in claim 15 and "the substance inhibiting expression or activity" in claim 26 is totally unknown. Thus, the descriptions of these claims are extremely unclear. Accordingly, no meaningful search on the above claims is possible.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 15, 23-26.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP03/10131

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☒ not complied with for the following reasons:

Although the methods according to claim 1 have the matter in common that they are "methods of judging an inflammatory disease which include detecting a gene polymorphism occurring in a region of about 130 kb of 6p21," a method of judging an inflammatory disease by detecting a polymorphism in LT-α gene was publicly known before the priority date of the present application (see, if necessary, Thrombosis Research, November 2000, Vol. 100, No. 4, pages 263-269).

Thus, the inventions of claim 1 as a whole are regarded as neither making a contribution to the prior art nor having a technical relationship involving one or more of the same or corresponding technical features and so they are not considered to be a group of inventions so linked as to form a single general inventive concept. The same applies to the claims other than claim 1.

Accordingly, "a method of judging an inflammatory disease which includes detecting a polymorphism in LT-α gene," "a method of judging an inflammatory disease which includes detecting a polymorphism in IKBL gene" and "a method of judging an inflammatory disease which includes detecting a polymorphism in BAT1 gene" are each regarded as a single invention, and the number of inventions of the present application is considered to be three.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-14, 16-22, 27-32.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/JP03/10131

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-7, 10-14, 16-22, 27-32	YES
	Claims	8-9	NO
Inventive step (IS)	Claims		YES
	Claims	1-14, 16-22, 27-32	NO
Industrial applicability (IA)	Claims	1-14, 16-22, 27-32	YES
	Claims		NO

2. Citations and explanations

Document 1: Thrombosis Research, 2000, Vol. 100(4), pages 263-269, full text; See the whole paper.
Document 2: Atherosclerosis, 2001, Vol. 154(3), pages 691-697; See the whole paper.
Document 3: Atherosclerosis, 2001, Vol. 159(1), pages 137-144, See the whole paper.
Document 4: Human Immunology, 1999, Vol. 60, pages 1128-1130, full text
Document 5: The Journal of Experimental Medicine, 1991, Vol. 173(1), pages 209-219, See the whole paper and particularly Fig. 3.

Document 1 describes that the polymorphisms in -308 (A→G) of TNF-α and in +252(A→G) of LT-α have some relation with myocardial infarction and that the polymorphisms are determined by PCR using a primer.

Document 2 describes that polymorphisms occurring in -308 TNFA, the promoter region of TNF, and the first intron of lymphotoxin-α relate to inflammatory diseases, and reference is made specifically to the relation of myocardial infarction and coronary thrombosis to the polymorphisms. It is also described that the genotype of TNF-β is determined by PCR using a primer.

Document 3 describes that the single nucleotide polymorphisms of IL-10, TNF-α and TNF-β relate to the risk of coronary diseases and myocardial infarction and cites 252G/A as the polymorphism of TNF-β. Further, it is described that the polymorphisms are determined by PCR using a primer.

Document 4 describes that two polymorphisms (-308 and -238) occurring in the promoter region of TNF-α and a polymorphism (+252) occurring in the first intron of TNG-β relate to systemic sclerosis. It is mentioned that the genotypes of the polymorphisms are determined by PCR using a primer.

The regions of the TNF-β polymorphisms are shown specifically in Fig. 3 of document 5.

In view of documents 1-4, the subject matters of claims 8 and 9 do not appear to be novel.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of : V.2

As described in documents 1-4, the G/A polymorphism occurring in +252, the 90th of the first intron in a lymphotoxin-α gene, relates to inflammatory diseases such as myocardial infarction, and the method of determining the polymorphism by PCR using a primer were publicly known before the priority date of the present application and so it is considered that a person skilled in the art could have easily conceived of judging an inflammatory disease by detecting the polymorphism occurring in a lymphotoxin-α gene. TNF-β, i.e., the base sequence of lymphotoxin-α, and the region of its polymorphism were also publicly known before the priority date of the present application as described in document 5. Therefore, obtaining a probe which hybridizes with the base sequence containing the polymorphism or its complementary sequence, and a primer for amplifying the sequence containing the polymorphism or its complementary sequence are matters usually practiced by a person skilled in the art. Making a kit for detecting inflammatory diseases with the probe and the primer and analyzing the expression of a lymphotoxin-α gene by the use of the probe and the primer could also have been easily conceived of by a person skilled in the art. Further, it is considered that a person skilled in the art could have easily arrived at the measurement of transcriptional activity and the screening of transcriptional activity inhibitors by using a cell into which a fragment of a lymphotoxin-α containing the abovementioned polymorphism is transferred.

Accordingly, it is considered that a person skilled in the art could have easily arrived at the subject matters of claims 1-14, 16-22, and 27-32 on the basis of documents 1-5.